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(54) Title: THERAPEUTIC PREPARATION COMPRISING SHARK CARTILAGE

(57) Abstract

The present invention relates to a composition comprising shark cartilage and a natural oil, and to medical treatments using such a composition. In particular, the invention relates to a composition comprising shark cartilage and emu oil, which is useful for the treatment of injuries or disorders to the epithelium, skin or joints. More particularly, the present invention relates to the use of the shark cartilage and emu oil composition in the treatment of burns, cancer and inflammation, particularly in humans.

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Therapeutic Preparation Comprising Shark Cartilage

Field of the Invention

The present invention relates to a composition comprising shark cartilage and a natural oil, and to medical treatments using such a composition. In particular, the invention relates to a composition comprising shark cartilage and emu oil, which is useful for the treatment of injuries or disorders to the epithelium, skin or joints. More particularly, the present invention relates to the use of the shark cartilage and emu oil composition in the treatment of burns, cancer, and inflammation, particularly in humans.

Background of the Invention

In recent years there has been an enormous expansion of interest in the use of natural substances in the sciences of pharmacy and pharmacology. Each year many new natural substances are isolated from natural sources such as plants, micro-organisms and animals such as marine organsims.

Pharmaceutical and therapeutic compositions or preparations based on natural substances are often popular with the general public, due to the perception that natural products are of superior quality or less likely to have contraindications compared to equivalent chemical products synthesised in a laboratory. The high regard for natural substances for use in pharmaceutical and therapeutic compositions or preparations is reflected in the continuing popularity through the centuries of homoeopathic medicine and natural remedies such as those used in Asia and Eastern Europe.

Accordingly, many commercially available pharmaceutical and therapeutic compositions or preparations now comprise natural products. These natural products are generally isolated in powdered or liquid form and the range of natural products available is enormous. Extracts have

been prepared from innumerable plant species such as aloe vera, Kola, garlic, ginseng, ginger and tamarind plants. Other sources of natural products are as diverse as bee pollen, fish liver and seaweed.

Of particular interest as a pharmaceutical or therapeutic agent is shark cartilage. Sharks do not have a bony skeleton, but instead have a cartilaginous skeleton which can be processed to form a white powder. Shark cartilage comprises protein/mucopolysaccharide complexes, in which the protein is predominantly Type II collagen. The main mucopolysaccharides in the cartilage are glycosaminoglycans such as chondroitin sulphate, heparin, dermatan sulphate, keratin and hyaluronan.

In China, shark's fin soup has been eaten for centuries because of its reputed therapeutic properties, and particularly for its reputed action as a cancer prophylactic. In recent times numerous research papers have been published regarding the therapeutic effects of shark cartilage.

Without wishing to be bound by theory, it is believed that shark cartilage may stimulate the cellular and humoral components of the immune system. This makes shark cartilage effective against bacterial, viral and fungal infections, and consequently may provide support to the immune system against colds, influenza and other infections.

Shark cartilage has also been shown to contain powerful anti-inflammatory agents, and to provide wound healing. Consequently it is believed that shark cartilage may provide a source of relief from the effects of degenerative bone and joint disorders such as arthritis, rheumatoid arthritis, osteoarthritis and sports-related injuries.

Shark cartilage also contains an anti-angiogenesis factor, which inhibits the growth of new blood vessels. Accordingly, shark cartilage may be utilised as a cancer treatment by inhibiting the vascularisation of

tumours.

One of the problems associated with the use of shark cartilage relates to the inability to deliver sufficient amounts of shark cartilage components to a patient to provide an effective dose.

This is illustrated in an article by Prudden and Balassa in "Seminars in Arthritis and Rheumatism" (Volume III, Number 4-Summer 1974, pp287-321) which discloses the administration to a patient afflicted with progressive systemic sclerosis (PSS), a connective tissue disease, of a 5% solution of sterile high temperature aqueous cartilage extract by subcutaneous injection. In this trial the patient received between 50 and 400 ml of a 5% extract per month. The article reports that some improvement was noted in the patient's skin flexibility and thickness, but does not indicate any significant alleviation of the limited range of motion in the limbs that is a common feature of the disease. Also, it did not comment on any improvement or effect on gastric-intestinal function or respiratory efficiency, both of which are adversely affected by this systemic disorder. The patient received the equivalent of between about 2½ and 20 grams per month of finely-divided cartilage powder by the parenteral route. In most instances, it was necessary to admit the patient to the hospital to be administered the large volumes of liquid medication that were required. The article by Prudden et al suggests that parenteral administration of the active agent in a liquid dosage form is required to facilitate transport of the agent throughout the body.

The treatment disclosed in the preceding article does not lend itself to self-administration by the patient on a long-term basis, utilises a pharmaceutical formulation that is relatively expensive to prepare (due to the need for extraction at high temperature and under high pressure), and is limited to administration of relatively low quantities (between about 2½ and 20 grams) of active agent per month.

Other routes that have been used to deliver shark cartilage components include rectal and vaginal administration. While these routes allow greater volumes of shark cartilage to be delivered, the ability to deliver optimal quantities of shark cartilage, namely, 60 to 100 grams per day, is practically impossible via these routes. Furthermore, patients report discomfort and feelings of invasion, when shark cartilage is delivered vaginally or anally. Therefore, while shark cartilage is known to have potential benefit as an anti-inflammatory agent, anti-angiogenesis agent and agent for the stimulation of the cellular and humoral components of the immune system, it has not hitherto been successfully or widely used for these applications because it has not been possible to achieve suitable levels of tissue penetration, particularly skin penetration.

One approach which has recently been investigated is topical application. Attempts have been made to combine shark cartilage with a variety of chemical vehicles, particularly oils, but with limited success. Therefore, there are still problems associated with the delivery of shark cartilage as a topical application, and there is an inability to obtain sufficient amounts of shark cartilage in a suitable carrier that enables the material to be readily absorbed through the skin. Thus, there is a requirement in the art for a carrier which is capable of delivering an effective amount of shark cartilage to the skin such that it is readily absorbed through the outer layers. Furthermore, there is a requirement for a preparation which is more stable over time.

Natural oils are particularly popular components for pharmaceutical and therapeutic compositions or preparations. These include a vast range of plant derived oils such as evening primrose, coconut, palm, guaiac wood, citrus, origanum, patchouly, rose, sweet birch, rose oil, tagetes, cloves and costus oils. Commonly used fish oils include cod liver oil and shark liver oil. In recent times

animal oils have not generally been as popular as fish oils or plant oils for pharmaceutical and therapeutic compositions, particularly for oral administration, because they generally have high saturated fat levels and high cholesterol levels which are perceived by the general public as "unhealthy". However some animal oils such as goanna oil and emu oil appear to have avoided this label.

Emu oil is an opaque whitish solid of waxy texture derived from the flesh, particularly the fat, of emus, and has an excellent ability to penetrate skin.

Emu oil is predominantly lipid, mainly in the form of triacylglycerols, with free fatty acids as a minor component (up to about 10%). The majority of the fatty acids are monounsaturated (about 51-55%) or saturated fatty acids (about 37-38%); a minority are polyunsaturated fatty acids (about 7-12%). The cholesterol levels of such oils is about 200-300 micrograms/gram oil, which is lower than those of fish-derived oils.

The fatty acid profile of emu oil is similar to that of many of the oils of plant origin such as evening primrose oil, coconut, palm, sunflower and canola. As oils of plant origin are already widely produced at relatively low cost and used in large volumes in foodstuffs and pharmaceutical or therapeutic compositions, there has not hitherto been a great incentive or need to include emu oil in these types of composition or preparations. Emu oil available commercially is commonly sold as a liniment or emollient.

Surprisingly, it has now been found that a pharmaceutical and/or therapeutic composition comprising natural substances and having exceptional skin penetrating and physiological response characteristics can be provided by the combination of shark cartilage and emu oil. The composition can be formed into an easily applied, stable product with a shelf life of at least 12 months.

Accordingly, the present invention attempts to overcome or at least alleviate some of the problems

associated with providing a composition comprising natural substances for use in treating one or more types of injuries or disorders, particularly, injuries or disorders of the epithelium, skin or joints.

Finally, throughout the description and claims of this specification, the word "comprise" and variations of the word, such as "comprising" and "comprises", means "including but not limited to" and is not intended to exclude other additives, components, integers or steps.

Summary of the Invention

The present invention provides a composition comprising shark cartilage, natural oil and a pharmaceutically acceptable carrier, wherein the composition is readily absorbed into animal tissue.

Preferably, the natural oil is emu oil.

According to another aspect of the present invention there is provided a method of treating an injury or disorder comprising the step of administering or applying to a patient in need thereof an effective amount of a composition comprising, shark cartilage and emu oil.

According to another aspect of the present invention there is provided a method of preparing a composition for the treatment of an injury or disorder, comprising the step of mixing shark cartilage and emu oil.

The emu oil and shark cartilage in combination exhibits superior tissue penetration and superior physiological response compared to the tissue penetration of shark cartilage (and perhaps also emu oil) alone. Without wishing to be bound by theory it is believed that emu oil may increase the tissue penetration and/or act as an adjuvant for the shark cartilage. Shark cartilage may also have a similar effect on the emu oil.

The combination of substances to provide beneficial synergistic effects is a known phenomenon, however the reasons for this phenomenon are not always known, nor is the synergy always predictable. The

interaction between chemical species in a pharmaceutical or therapeutic composition can be affected by a multitude of factors, such as solubility of one species in another, acid-base and pH effects, other solubility phenomena, electrolytic effects, cationic-anionic interactions, and stereochemical effects.

With respect to prior art preparations combining shark cartilage with a lipid, these have not exhibited the tissue penetration in conjunction with the improved physiological response exhibited by the composition of the present invention.

Preferably, the emu oil for use in the composition of the present invention is prepared by a process which comprises a fat-reducing stage and an oil reduction stage. It is particularly preferred that there is no water contamination in the fat-reducing stage, and that the oil extraction is carried out at low temperature.

Preferably, the shark cartilage for use in the composition of the present invention is prepared by a process which comprises a drying stage and a milling stage. It is particularly preferred that the drying and milling are carried out at low temperature.

Preferably, the composition of the present invention comprises between 5 and 90 wt%, more preferably between 10 and 70 wt%, or even more preferably between 20 and 60 wt% shark cartilage. Most preferably 50% cartilage is used.

Preferably, the composition of the present invention comprises between 0.1 and 50 wt%, more preferably between 1 and 30 wt%, or even more preferably between 3 and 10 wt% emu oil.

Preferably, the composition of the present invention comprises between 30 and 60 wt% shark cartilage in combination with between 3 and 8 wt% emu oil.

Preferably, the shark cartilage and emu oil are mixed with one or more suitable, convenient or desirable components to form a suitable preparation or composition.

The components may for example be a suitable base, emollient, demulcent, emulsifier, preservative or other additive. Suitable components may for example, be chosen from the group consisting of; hydrocarbons such as paraffin, petrolatum, white petrolatum, mineral oil, light mineral oil, and hydrophilic petrolatum; animal fats such as anhydrous lanolin and lanolin; demulcents such as gums, mucilages or starches, including gum arabic, acacia syrup, gum tragacanth, licorice root, agar, sodium alginate, methylcellulose, sodium carboxymethylcellulose, glycerin, propylene glycol, polyethylene glycols, and tetraglycine; vegetable oils such as olive oil, cottonseed oil, corn oil, almond oil, peanut oil, persic oil and cocoa butter; inorganic additives such as zinc oxide, zinc sulphate, aluminium silicate; and combinations thereof.

For example, the shark cartilage and emu oil may be mixed with an existing pharmaceutical or therapeutic composition such as calamine lotion (essentially a pink insoluble powder of zinc oxide) or a common ointment base such as a combination of calamine (8 wt%), zinc oxide (2 wt%), 2 wt% glycerine in bentonite magma (native colloidal, hydrated aluminium silicate) or olive oil and rosewater, aloe vera, wattle oil, orange oil or other oil(s).

Preferably the composition of the present invention can be applied or administered in a number of suitable ways, for example topically. The composition can take any suitable form, such as ointments, pastes, lotions, creams, liniments and the like, including aqueous creams, lanolin based ointments and emulsions.

The method of application or administration of the preparation or composition is dependent on the dosage and concentration of the emu oil and shark cartilage in the composition, so that undesirable effects of the composition are taken into account. For example, it may be necessary to take into account any toxicity or hypersensitivity of the individual to shark cartilage or emu oil in certain concentrations and/or dosages. The method of application

and/or administration of the preparation or composition is determined so as to be efficient and efficacious without being harmful.

Preferably the preparation or composition of the present invention will be used for one or more of the following:

- as an anti-inflammatory agent such as for use in the treatment of skin, joint and muscular injuries such as sunburn and degenerative bone or joint disorders such as arthritis, rheumatoid arthritis and osteoarthritis;

- as an antibacterial, antiviral and/or antifungal agent such as for use in the treatment of immune system disorders and infections including colds and influenza; and

- as an anti-angiogenesis agent for the treatment of disorders such as haemorrhoids or tumours or carcinomas.

The pharmaceutical and/or therapeutic composition of the present invention typically finds application in the treatment of open wounds, haemorrhoids, skin cancers, burns, joint and muscle inflammation and tumours.

The present invention will now be described by way of example only with reference to the following non-limiting examples.

Example 1

A composition according to the present invention was prepared by the combination of shark cartilage (30 wt%) and emu oil (5 wt%).

The composition was applied to 20 human subjects suffering open anal wounds. All subjects reported that the composition reduced inflammation and redness associated with the wound and generally soothed the affected area.

Stimulation of the healing process was also noted.

Example 2

The composition of Example 1 was applied to haemorrhoids of 3 human subjects. Both subjects reported rapid contraction and disappearance of the haemorrhoids.

Example 3

The composition of Example 1 was applied to several basal cell carcinomas of 4 human subjects. The redness and size of the carcinomas appeared to be reduced.

Example 4

The composition of Example 1 was applied to an ulcerated flesh wound of a subject which eventually healed. The quality of the skin growth was of superior quality and appearance to a similar wound on the same subject which was left to heal without the application of the composition of the present invention.

Example 5

The composition of Example 1 was topically applied to 3 subjects by a professional masseur. The subjects reported reduced redness and inflammation in joints and injured muscles to which the composition was applied.

Example 6

The composition of Example 1 was topically applied to 6 subjects with severe sunburn. The subject reported that the soreness associated with the sunburn was gone within 30 minutes and the following day there was virtually no redness and inflammation. The subject did not peel.

Example 7

A composition according to the present invention

was prepared by the combination of shark cartilage (50 wt%), emu oil (5 wt%), food grade preservatives, food grade gel base, minor oils, alovera, wattle oil and orange oil. The components were mixed together at room temperature and no heat was supplied to the process.

The composition was used successfully in the treatment of skin rashes on dogs and horses.

Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. It is understood that the invention includes all such variations and modifications which fall within the spirit and scope as described.

CLAIMS

1. A composition comprising shark cartilage, natural oil and a pharmaceutically acceptable carrier, wherein the composition is readily absorbed into animal tissue.

2. A composition according to claim 1, wherein the natural oil is emu oil.

3. A composition according to claim 2, wherein the concentration of shark cartilage is between 5 and 90 wt% w/w.

4. A composition according to claim 3, wherein the concentration of shark cartilage is between 10 and 70 wt% w/w.

5. A composition according to claim 4, wherein the concentration of shark cartilage is between 20 and 40 wt%.

6. A composition according to any one of claims 2 to 5, wherein the concentration of emu oil is between 0.1 and 50 wt% w/w.

7. A composition according to claim 6, wherein the concentration of emu oil is between 3 and 10 wt% w/w.

8. A composition according to any one of claims 1 to 7, wherein the carrier is selected from the group consisting of hydrocarbons such as paraffin, petrolatum, white petrolatum, mineral oil and light mineral oil, hydrophilic petrolatum; animal fats such as anhydrous lanolin and lanolin; demulcents such as gums, mucilages or starches including gum arabic, acacia syrup, gum tragacanth, licorice root, agar, sodium alginate, methylcellulose, sodium carboxymethylcellulose, glycerin, propylene glycol, polyethylene glycols, tetraglycine; vegetable oils such as olive oil, cottonseed oil, corn oil, almond oil, peanut oil, persic oil and cocoa butter; inorganic additives such as zinc oxide, zinc sulphate, aluminium silicate and combinations thereof.

9. A composition according to any one of claims 1 to 8, wherein the composition is suitable for topical application.

10. A method of treating an injury or disorder comprising the step of administering or applying to a patient in need thereof an effective amount of a composition according to any one of claims 1 to 9.

11. A method according to claim 10, wherein the composition comprises emu oil.

12. A method according to claim 11, wherein the composition is used as an as an anti-inflammatory agent, anti-degenerative bone or joint disorders agent, antibacterial, antiviral, antifungal agent, or anti-angiogenesis agent.

13. A method according to claim 11, wherein the condition treated is selected from the group consisting of burns, joint and muscular injuries, degenerative bone or joint disorders, arthritis, rheumatoid arthritis, osteoarthritis, haemorrhoids,and cancers.

14. A method of preparing a composition for the treatment of an injury or disorder, comprising the step of mixing shark cartilage and emu oil.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 98/00760

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: A61K 35/60

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC Cl[6]: A61K 35/60

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
AU: IPC as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT, JAPIO : shark: and cartilag:
CA, Medline : shark: and cartilag: and oil

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96/23512 A (LES LABORATOIRES AETERNA INC) 8 August 1996 See page 57	1,9,10
X	Patent Abstracts of Japan, JP 07-308169 A (HAPUTO INTERNATL:KK, PETSUKAA:KK) 28 November 1995 Abstract	1,7,10
A	US 4444752 A (PRUDDEN) 24 April 1984 See whole document	

[X] Further documents are listed in the continuation of Box C

[X] See patent family annex

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 November 1998	18 NOV 1998
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929	Authorized officer **TAMARA NIZNIK** Telephone No.: (02) 6283 2422

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 98/00760

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SCIENCE, volume 221, no 4616, 16 September 1983 Lancaster, PA US, pages 1185-1187, ANNE LEE et al "Shark Cartilage Contains Inhibitors of Tumor Angiogenesis" See whole document	
A	FED.PROC. volume 45, no 4, 1986 page 949 C.A.LUER "Inhibitors of Angiogenesis from Shark Cartilage" Abstract 4624	

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/AU 98/00760

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
WO	96/23512 A	AU	23001/95	AU	37388/95	BG	100941
		BG	101870	BR	9507552	BR	9510540
		CA	2188793	CA	2212010	CZ	9603141
		CZ	9702452	EP	759765	EP	806960
		FI	964327	FI	973195	HU	76554
		HU	77488	NO	964547	NO	973564
		NZ	284407	PL	317076	PL	321678
		US	5618925	WO	95/32722		
JP	07-308169	NONE					
US	4444752	NONE					

END OF ANNEX

DERWENT-ACC-NO: 1999-254324

DERWENT-WEEK: 199933

TITLE: Topical compositions useful for treating injury or disorders of the epithelium, skin or joints

INVENTOR: ATTARD R J; DELACRETAZ P A ; DRINKWATER J A

PATENT-ASSIGNEE: MICRONIZED FOODS PTY LTD[MICRN]

PRIORITY-DATA: 1997AU-009205 (September 16, 1997)

PATENT-FAMILY:

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WO 9913891 A1	March 25, 1999	EN
AU 9890553 A	April 5, 1999	EN

DESIGNATED-STATES: AU CA US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-DATE
WO1999013891A1	N/A	1998WO-AU00760	September 16, 1998
AU 9890553A	Based on	1998AU-090553	September 16, 1998

INT-CL-CURRENT:

TYPE	IPC DATE
CIPS	A61K35/60 20060101

ABSTRACTED-PUB-NO: WO 9913891 A1

BASIC-ABSTRACT:

NOVELTY - Composition comprising shark cartilage, natural oil and a carrier, is readily absorbable transdermally.

None given.

USE - The compositions are useful for treating injuries and disorders of the epithelium, skin or joints. The composition comprising shark cartilage and emu oil is useful as an antiinflammatory, antibacterial, antiviral, antifungal or antiangiogenesis agent, and for treating burns, joint and muscular injuries, degenerative bone or joint disorders, arthritis, rheumatoid arthritis, osteoarthritis, haemorrhoids and cancers.

ADVANTAGE - The compositions have exceptional skin penetrating activity.

EQUIVALENT-ABSTRACTS:

PHARMACEUTICALS

Preferred Composition: The natural oil is preferably emu oil, and the carrier is a hydrocarbon (e.g. paraffin, petrolatum, mineral oil, light mineral oil or hydrophilic petrolatum); animal fat (e.g. anhydrous lanolin or lanolin); demulcent (e.g. gum, mucilage or starch); vegetable oil (e.g. olive oil); inorganic additive (e.g. zinc oxide). The composition comprises: shark cartilage 5-90 (preferably 20-40) wt.% and emu oil 0.1-50 (preferably 3-10) wt.%.

POLYMERS

Preferred Carrier: The carrier is selected from gum, mucilage or starch such as gum arabic, acacia syrup, gum tragacanth, licorice root, agar, sodium alginate, methylcellulose, sodium carboxymethylcellulose, glycerin, propylene glycol, polyethylene glycols, and/or tetraglycine,

Administration is preferably topical.

A composition comprising shark cartilage (30 wt.%) and emu oil (5 wt.%), was applied to an ulcerated flesh wound. When the wound healed, the skin growth was of superior quality and appearance to that of a similar wound which was left to heal without application of the composition.

TITLE-TERMS: TOPICAL COMPOSITION USEFUL TREAT INJURY DISORDER EPITHELIUM SKIN JOINT

DERWENT-CLASS: A96 B04 C03 C04

CPI-CODES: A12-V01; B04-B01C; B04-B04M; B05-A03A; B10-A07; B10-E04C; B12-M02F; B14-A01; B14-A02; B14-A04; B14-C03; B14-C09; B14-E04; B14-H01; B14-N01; B14-N17A; C04-B01C; C04-B04M; C05-A03A; C10-A07; C10-E04C; C12-M02F; C14-A01; C14-A02; C14-A04; C14-C03; C14-C09; C14-E04; C14-H01; C14-N01; C14-N17A;

CHEMICAL-CODES: Chemical Indexing M1 *01* Fragmentation Code M431 M782 P714 P943 Q140 Specific Compounds RA0217 Registry Numbers 102715

Chemical Indexing M1 *02* Fragmentation Code M431 M782 P714 P943 Q140 Specific Compounds RA0218 Registry Numbers 103242

Chemical Indexing M1 *03* Fragmentation

Code M431 M782 P714 P943 Q140 Specific Compounds RA0219 Registry Numbers 103672

Chemical Indexing M1 *04* Fragmentation Code M431 M782 P714 P943 Q140 Specific Compounds RA03SP Registry Numbers 111074

Chemical Indexing M1 *05* Fragmentation Code M431 M782 P714 P943 Q140 Specific Compounds RA021C Registry Numbers 87005

Chemical Indexing M1 *06* Fragmentation Code M431 M782 P714 P943 Q140 Specific Compounds RA01PZ Registry Numbers 91676

Chemical Indexing M1 *07* Fragmentation Code M431 M782 P714 P943 Q140 Specific Compounds RA021E Registry Numbers 91613

Chemical Indexing M1 *08* Fragmentation Code M431 M782 P714 P943 Q140 Specific Compounds RA00GT Registry Numbers 200757 200799

Chemical Indexing M1 *09* Fragmentation Code M431 M782 P210 P241 P421 P714 P941 P942 P943 Q140 Specific Compounds RA00NG Registry Numbers 103243

Chemical Indexing M1 *10* Fragmentation Code M431 M782 P210 P220 P241 P420 P421 P714 P941 P942 P943 Q140 Specific Compounds RA00NG Registry Numbers 103243

Chemical Indexing M1 *15* Fragmentation Code J0 J011 J2 J221 J5 J581 K0 K4 K421 L5 L560 M210 M211 M262 M280 M281 M320 M423 M431 M782 P714 P943 Q140 Specific

Compounds R24070 Registry Numbers 86729

Chemical Indexing M1 *16* Fragmentation Code A111 A960 C710 J0 J011 J1 J111 M423 M431 M782 P714 P943 Q140 Specific Compounds R06725 Registry Numbers 107307 133925 134009 89822

Chemical Indexing M1 *17* Fragmentation Code A111 A960 C710 H5 H521 H8 J0 J011 J1 J171 M280 M311 M321 M342 M349 M381 M391 M423 M431 M630 M782 P714 P943 Q140 Specific Compounds R07352 Registry Numbers 133912 133998 140011 140012 190069

Chemical Indexing M1 *18* Fragmentation Code J0 J011 J1 J111 K0 L8 L811 L814 L815 L817 L831 L832 M423 M431 M782 P714 P943 Q140 Specific Compounds R24037 Registry Numbers 96536

Chemical Indexing M2 *11* Fragmentation Code A430 A940 C108 C316 C540 C730 C801 C802 C803 C804 C805 M411 M431 M782 P714 P943 Q140 Specific Compounds R01741 Registry Numbers 132889 1577

Chemical Indexing M2 *12* Fragmentation Code A430 A940 C108 C550 C730 C801 C802 C803 C804 C805 C807 M411 M431 M782 P714 P943 Q140 Specific Compounds R01520 Registry Numbers 866

Chemical Indexing M2 *13* Fragmentation Code H4 H403 H483 H8 M280 M313 M321 M332 M343 M383 M391 M416 M431 M620 M782 P714 P943 Q140 Specific Compounds R00113 Registry Numbers 490

Chemical Indexing M2 *14* Fragmentation

Code H4 H402 H482 H8 M280 M313 M321 M331 M342 M383 M391 M416 M431 M620 M782 P714 P943 Q140 Specific Compounds R00137 Registry Numbers 861

Chemical Indexing M6 *19* Fragmentation Code P210 P220 P241 P420 P421 P714 P941 P942 Q140 R263

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Polymer Index [1.2] 018 ; ND01; Q9999 Q8037 Q7987;

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